CONCERNING A DISTINCT TYPE OF HYPERNEPHROMA OF THE KIDNEY, WHICH SIMULATES VARIOUS CYSTIC CONDITIONS OF THAT ORGAN.

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THE pathological diagnosis of tumors of the kidney has made notable and permanent advances within recent years. In addition to the old and well recognized types of sarcoma and carcinoma among the malignant neoplasms which affect that organ, the so-called teratomata, which often assume many of the clinical characters of malignancy, have come to be definitely established. Of these, at least three types are known —the embryomata, or " Wilms' tumors," containing glandular tissue, striated muscle, and occasionally other elements; the adeno-sarcomata of Birch-Hirschfeld, grouped by many authors as tumors of the Wolffian duct, [2, 5] by others as a species of the Wilms' tumors; [1 2] and the Grawitz tumors, or hypernephromata. These various types of new growths possess certain characteristics of their own, both in their clinical course and in their prognosis, which renders their recognition an extremely important object in diagnosis; and yet it cannot be gainsaid that this recognition still remains in very many of the cases little less than a diagnostic impossibility. The cause of this difficulty is not very far to seek, for, as pointed out by Thorndike, in almost all the recent publications which deal with these growths, their histological features have been made the subject of elaborate study and description, almost to the complete exclusion of their clinical characteristics. It would seem, however, that the time had arrived when a more careful study and definition of the latter aspect of the problem might be fruitful in practical results. It is quite evident that tumors which differ so markedly in their course, their prognosis and, under certain conditions, in the indications for treatment cannot be profitably thrown together in the nondescript category of malignant neoplasms of the kidney.

In the following paper, an attempt has been made to define a certain group of hypernephromata, which offer many difficulties in the way of diagnosis, and yet which seem, upon closer analysis, to present certain peculiar characteristics, which are sufficiently individual to render their recognition possible.

An example of this group is offered by a very typical case which was recently observed in the German Hospital in New York City. The patient, E. W., a man 56 years of age, was admitted to the hospital in June, 1904. For the following details I am largely indebted to Dr. Kammerer, in whose ward he lay, and also to Dr. H. Klein,[6] who had previously presented him at a meeting of the German Medical Society for diagnosis. His family history is irrelevant. His personal history up to the age of 16 makes mention only of the diseases of childhood. At the age of 16 or 17, he had an attack of hæmaturia, which lasted for almost two weeks. At this time he had no pain, and no other evidences of disease. From that time until 1899, a period of thirty-five years, the patient remained in every respect perfectly healthy, so far as he knew. In November, 1899, he again observed the presence of blood in the urine, which persisted for several weeks, and led him to seek the German Hospital in December. His only complaint at that time was weakness and occasional vertigo, due probably to the loss of blood. He had no pain either during or after urination. His urine at that time contained red cells, epithelia, leucocytes, and a few hyaline casts, and measured 1300–1500 cc. per day. He remained in the hospital for about five weeks, during which time the urine gradually cleared up, and in January, 1900, he left, apparently cured. He had presented no œdema and no uræmic symptoms of any kind. No clinical diagnosis was noted. About a year later he had an exactly similar attack, which lasted four to six weeks, and since then three more attacks, at intervals of several months. In general, these attacks were all of similar nature, and each one left him weaker and more anemic than before, so that for a year previous to his admission to the hospital he had been unable to follow any occupation. In March, 1903, he first noticed an increase in the size of his abdomen, which steadily progressed. This went hand in hand with a sense of fulness and of oppression in the epigastrium after eating, and with a gradual diminution of appetite. During this period the patient thinks that he lost about ten pounds in weight. He has suffered from constantly increasing weakness, vertigo, and other anemic symptoms, which have always been aggravated just prior to the onset of his hematurias. He has never passed a stone or gravel, and has never had any form of colic.

Physical examination.—Man of medium height, with poor skeletal and muscular development. Considerable emaciation. Pallor of skin and visible mucous membranes marked. No œdema over malleoli or sacrum. Examination of the thorax reveals nothing of note, except slight upward displacement of the apex beat, and a few rales at the bases, especially marked on the left side. The abdomen is markedly distended, especially on the left side, and there are large and torturous veins in the skin of that side of the abdomen. By palpation, a tumor mass is found to occupy practically the entire left side of the abdomen, extending well beyond the middle line, including the entire umbilical and upper part of the pubic regions, and left lateral portions of the abdomen. In the midsternal line, it can be felt as high as three fingers' breadth below the ensiform, and as low as four fingers' breadth below the umbilicus. It appears to be smooth, rounded, tense, but slightly fluctuating, and exhibits no respiratory mobility. It is not tender. The liver and spleen are not palpable. The percussion note over the mass is uniformly flat, except for a tympanitic band, presumably ascending colon, towards the left flank. It is separated by a narrow tympanitic zone from the area of liver flatness. No evidence of free fluid in the abdomen. The urine is dark red, opaque, and contains coagula; albumen is present in varying amounts. Microscopically, numerous red blood cells, leucocytes, and epithelia; also hematoidin, and triple phosphate crystals. Cystoscopic examination revealed normal urine issuing from the right ureter, a bloody fluid from the left. A blood examination made shortly after admission showed 60 per cent. of hemoglobin; less than 3,000,000 red cells; 7800 whites, of which 40 per cent. are mononuclears.

The red cells were not normal; there were some poikilocytosis, a few macro- and micro-cytes, but no nucleated reds. Examination of the fluid obtained by puncture of the mass revealed only red blood cells, leucocytes, and degenerated epithelia. Pulse ranged from 90 to 100, temperature from 99° to 101°.

On June 11 Dr. Kammerer removed the tumor by lumbar incision.

Macroscopically it presents * a large cystic mass, irregularly ovoidal in shape. The surface is smooth, glistening, and white in color, and covered with a network of injected veins. There are surface indications of lobulation. Upon section, the content is found to be a reddish brown, grumous fluid, which shows degenerated leucocytes, red cells, epithelia, numerous cholesterin crystals, and blood pigment. The wall, which seems to be composed of tough, dense, connective tissue, measures from 4 to 16 millimeters in thickness. Incomplete septa partially divide up the cavity of the cyst. The inner surface is smooth and covered with adherent fibrinous masses. Coursing in the wall of the cyst is found the thickened but patent ureter. To all appearances, the tumor is a large monolocular cystlike distension of the kidney, containing much altered blood. Closer examination reveals the presence of two inconspicuous strands of a different tissue, one of which lies in the capsule, the other in one of the septa. Both of these strands are enclosed in a distinct fibrous capsule. Their tissue is firm, their color yellow. On microscopic examination, they are found to be composed of adrenal tumor tissue, presenting the characters of this tissue as it appears after it has undergone malignant degeneration. In some places it is with difficulty distinguishable from cancer, while in others it unmistakably displays the characteristics of the adrenals. The wall proper of the cyst is found to contain the remains of kidney tissue—Malpighian bodies and tubules in a fairly intact condition, imbedded in a large amount of interstitial connective tissue.

The tumor falls, therefore, in the group of hypernephromata. It is differentiated, however, from the great majority of tumors of this class by its remarkable cystic char-

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* The tumor, with sections, was shown before the Pathological Society of New York in January, 1905, and is reported in Volume IV of the Proceedings, p. 156.[14]

acter. As is well known, all hypernephromata tend, from a variety of causes, to break down and form cysts. Almost invariably, however, there results a predominantly solid tumor, containing numerous larger or smaller, irregular, cyst-like, cavities; very rarely does the process give rise to the formation of single very large cysts, with hardly discoverable remmants of the tumor tissue in its walls. Nevertheless, a number of other cystic tumors have been described, presenting exactly similar characteristics and with similar hypernephromatous remmants in their walls, so that this—the cyst hypernephroma—must be recognized as one of the pathological varieties of that class of tumors.

The pathogenesis of these cysts seems to me to be a matter of some interest. The occurrence of adrenal tissue in the walls of the cysts seems to indicate with certainty their origin from adrenal "rests," and it might not at first sight seem unreasonable to suppose that their cystic character may simply represnt a further extension of the tendency, so common in hypernephromata, towards cystic degeneration.

On the other hand, they differ very markedly from the typical cystic hypernephromata in the fact that the latter never break down to form single large cystic tumors, but simply contain cystic cavities in the mass of the growth. Indeed, it is difficult to conceive of the complete destruction of the tissue of a hypernephroma, and its substitution by a cyst corresponding to the condition in the cases described. On the other hand, it is easy to see the analogy between these cysts and certain other structures described by W. C. Bosanquet[1] as "cystic adenoma of the adrenal." This author described the following condition: "A round mass lying in front of the left kidney, with the descending colon passing down on the outer side. On removal this proved to be a nearly spherical body, three inches to three and a half inches in diameter, slightly longer in a vertical than in a transverse direction. The left suprarenal was attached to the upper and back part of the tumor, and looked normal." The tumor was found to be a cyst. The cyst wall showed adrenal tissue, and its contents were of the consistency of jelly and orange colored. There is little doubt, as pointed out by Bosanquet, that the case described by Lockwood[8] is an example of the same condition; he also cites several other cases. It is probable, therefore, that the adrenal rests incorporated in the kidney have gone on, in the cases described in this paper, to the formation of "cystic adenomata" and not of hypernephromata, and have then eventually burst into the pelvis, and induced dilation of the entire organ. All the stages of this process may be traced in the cases which have been reported, starting with that of Leopold (Case VII), and ending with Case I.

With the purpose of establishing the clinical type which characterizes this group of hypernephromata, I have collected all the cases which I could discover in the literature. In all, five cases were found, which closely resembled the present case in their essential pathological features, and in the identification of adrenal tissue in the wall of the cysts. All of these cases, of course, have been reported since the publication of Grawitz's original paper in 1883.

CASE I (GRAWITZ[4]).—The patient, a well nourished man, was observed for ten years. The first symptoms of disease referable to the genito-urinary tract occurred at the age of 40. At this time there were vague urinary symptoms, diagnosed as pyelitis. Seven years later there was hematuria, which lasted a few days, and frequently recurred. The urine showed not only blood, but peculiar papilliferous masses, of which the cells were large and ovoidal, so that the diagnosis of carcinoma of the bladder was made. The patient, however, became better again, and only two years later observed a swelling in the left side of abdomen. This tumor continued to grow, and finally after two more years produced pressure symptoms. The latter were relieved on three successive occasions by puncture, the last of which set up a suppuration. The puncture fluid was chocolate-brown in color, cloudy, and contained many cholesterin crystals.

The autopsy, by Grawitz, disclosed a tumor mass in the left side of the abdomen, measuring 25 x 20 cm. The tumor proved to be a degenerated left kidney, transformed into an enormous monolocular cyst. The wall of the cyst showed remnants of kidney tissue, and remains of a whitish, crumbly tissue, which represented all that remained of the hypernephroma. There were three adrenal tumors in the opposite kidney.

CASE II (STRÜBING[10]).—In a patient, male, aged 67, a tumor of the abdomen was accidentally discovered. Tumor was clinically diagnosed to be cystic, derived from right kidney. General condition very good. Pressure symptoms involved the gastric and respiratory functions; and there was œdema of legs. The cyst was observed for four years to gradually increase in size. Hematuria never occurred. Remarkable is the absence of hematuria, in spite of patency of connection between cyst and ureter. Finally puncture was indicated to relieve the pressure symptoms, and evacuated 3 liters of a chocolate-brown fluid, mixed with fat and cholesterin. After a brief period of improvement, the cyst again began to grow rapidly, owing, as the autopsy showed, to hemorrhage, and the patient died from asthenia.

Autopsy.—A cystic tumor in right side of abdomen, measuring 22 x 24 x 26 cm. Contained 5 to 6 liters of dark, chocolate-brown, fluid; cholesterin crystals present. Cyst is composed of right kidney. Wall shows remnants of kidney tissue; pelvis and calices dilated; ureter enters cyst. Wall of cyst 4-5 mm. thick. The inner surface presents numerous nodules, ranging in size from pea to twice that of a walnut, whitish yellow in section. Wall microscopically composed of dense connective tissue. The small tumors consist of polygonal, epithelioid cells, with much fat contents. The diagnosis of hypernephroma was made from sections of these tumors. The left adrenal was normal.

CASE III (STRÜBING[10]).—A woman, aged 64, who had always been strong and healthy, had a sudden attack of pain in the left side. The pain lasted only a few days, but was followed by a period of irregular fever (37.2–38.8) and digestive disturbances. Examination disclosed a tumor of the size of a fist in the left hypochondrium. It was rounded, soft, not tender. It did not move with respiration. Tympany over the anterior surface. Urine normal. During the following three weeks, the tumor became larger and fluctuating; it reached the navel, and extended two fingers below the anterior spine. Fever persisted. Right pleurisy.

The case was diagnosed as a paranephritic abscess.

Lateral incision, for the purpose of drainage. Incision evacuated 1 liter of dark, bloody, fluid, containing large shreds of softened tissue. The tumor proved to be a large cyst. Suppuration followed, with pulmonary involvement, and death. The cyst was removed post-mortem and sent to Dr. Grawitz, who made the diagnosis of hypernephroma. The microscopic appearance was practically the same as that in the preceding case.

CASE IV (VILLARET[11]).—The clinical data are very inadequate. It is stated only that there were pressure symptoms from the tumor, but nothing referable to the urinary tract. The kidney was removed at operation, and came to the hands of Prof. Grawitz. The mass consisted of a sac, about as large as a man's head, the walls of which present soft tumor masses. At one point, kidney tissue is recognizable. The contents consist of a blood-stained fluid, containing masses of tissue in fatty degeneration, and much cholesterin. The wall shows remnants of kidney tissue, and adrenal tissue.

CASE V (PIRONE[9]).—A man of 40, previously healthy, began in January to have pains in the left side. At the same time a tumor made its appearance, and gradually increased in size. Three or four months later, the patient observed blood and clots in the urine. The clinical diagnosis was sarcoma of the left kidney. Extraperitoneal nephrectomy was done in June, 1902. At operation the mass was found to be fluctuating, and an exploratory puncture yielded about 100 cc. of a thick reddish brown liquid, containing granular material. Incision over the site of puncture yielded 150 cc. of detritus.

In addition to the five cases above detailed, in which adrenal tissue was identified in the wall of the cyst, the literature contains mention of a large number of other cases in which there is little doubt that the origin of the cysts was due to an unidentified hypernephroma of this type. These cases are not specifically referred to in the bibliography. A considerable number of them may be found in the article by Strübing who is, however, certainly somewhat too liberal in his interpretation of the pathology of certain of these doubtful cases. Two of these cases are of sufficient interest to demand detailed presentation.

Case VI (Schetelig"). — Patient is said to have had an enlarged abdomen from birth. This gradually increased in size up to the seventh year, when she had a severe fall. This was followed by a severe abdominal pain, and the passage of considerable quantities of bloody urine. This polyuria continued for three months and was associated with gradual decrease in the size of the abdominal tumor. The latter then gradually resumed its former size. At the age of ten the same thing recurred—a fall, hematuria, polyuria, decrease in size of tumor, and subsequent growth. Status praesens: a healthy looking young woman (age not given). Urine normal. Abdomen measures 122 cm. in its greatest diameter. A smooth, tense, movable tumor can be felt, apparently occupying the entire left half of the abdomen, and extending beyond the middle line to the right anterior superior spine. At operation, a median incision was made. The cyst was punctured, and 30 "pounds" of fluid evacuated. The fluid was rather dark in color, of a specific gravity of 1018, and contained large amounts of cholesterin. The patient recovered, but returned after three months with the abdomen again much swollen. A diagnosis was made of ovarian cyst, and the cyst was now extirpated by Esmarch.

The cyst was examined by Cohnheim. It measured more than one foot in diameter. The wall was composed of thick, leathery, whitish yellow membrane, almost ½ cm. in thickness. Here and there, it was studded with numerous smooth, whitish elevations, some of which were calcified in parts. The ureter was found running in the wall of the sac. There was no obstruction.

Case VII (Leopold[1]).—Woman, age 33. Has observed a swelling of the abdomen for five years. The objective signs were those of an enormous ovarian cystoma. An operation was done to extirpate this, and, upon removal, the following condition was found. The cyst was "the size of a man's head" and was found to be attached to the lower pole of a somewhat compressed right kidney. The kidney pelvis was quite intact, and the cyst nowhere communicated with it. The capsule of the kidney was continuous with that of the cyst. The content was bloody and contained much hematoidin. The origin of the cyst is held by Leopold to be doubtful.

If the present case be compared in its clinical features with the great majority of hypernephromata, it will be found to present certain peculiar characters of its own. Briefly, the hypernephromata, as a group, occur in middle life, they grow slowly, rarely, however, running for more than three years; their course may be marked by repeated attacks of sharp hæmaturia of brief duration; in most of the cases, metastases are a marked feature. Peculiar to the cyst-hypernephromata, as seen both in the case above described and in the other cases collated from the literature, are the clinical signs of a cystic, instead of a solid tumor of the abdomen; the prolonged period of growth,—in the case herein reported, over 40 years, if the first hæmaturia be counted, and five years during the second stage of growth; the character of the hæmaturias, which were very largely *on the presence or absence of hæmaturia.* In the the absence or very late occurrence of metastases; and the presence of pressure symptoms from the stomach, or other abdominal viscera, due to the large size of the cystic growth. This group of symptoms, if at all constant, would seem to afford a sufficiently characteristic syndrome. As regards the character of the urine, this is entirely determined by the anatomical relations of the tumor. It is a matter of great clinical importance, whether the cysts breaks into the pelvis of the kidney and forms one large cavity with it, which constantly discharges its contents into the ureter; or whether it intermittently discharges its contents into the ureter, a phenomenon characterized by an intermittent hæmaturia, as in the present case; or whether it causes lateral compression of the ureter, with retention of the cyst contents as in Case II; or whether it remains permanently separated, causing no urinary symptoms whatever as in Case VII.

If, now, the diagnosis of these tumors be considered, it is evident that they must be grouped, in the first place, among the intra-abdominal cysts. Further differentiation depends very largely *on the presence or absence of hæmaturia.* In the latter cases, the differential diagnosis from ovarian and other forms of cysts must be made largely from the location, the relation to the colon, and the other criteria upon which reliance is generally placed. Cases of this type have been confused with ovarian cyst and paranephritic abscess. If puncture of the cyst be made, a procedure of a very questionable character, the nature of the cyst fluid, which is uniformly rich in cholesterin and blood pigment, might be allowed to weigh heavily in favor of the diagnosis of cyst hypernephroma. In the former group of cases, the presence of hæmaturia, combined with the cystoscopic findings, make it a very simple matter to identify the renal origin of the tumor. In this case, therefore, the differential diagnosis must concern itself with all other forms of cysts, or cyst-like dilatations, of the kidney or pelvis associated with hæmaturia. If certain salient characters of the cyst hypernephromata—their prolonged course, their comparatively benign character, the absence of colic, their characteristic content of cholesterin and blood—be kept in mind, this diagnosis will rarely present great difficulties.

First to be considered is renal tuberculosis. Ordinarily, this produces only slight enlargment of the organ, perhaps to double its size; in another set of cases, it gives rise to large cyst-like dilatations, which may simulate an abdominal cystic tumor. The latter condition is due to intermittent or permanent obstruction of the ureter, either by stricture, or by caseous masses, resulting in a tuberculous pyonephrosis. At the same time, renal tuberculosis may produce recurrent hæmaturia, with emaciation, and anæmia, and so imitate in the most striking fashion the hypernephric cysts. There are generally marked vesical symptoms, such as frequent urination, and cystoscopic examination may then reveal ulcerations or other tuberculous lesions of the bladder. The presence of tubercle bacilli in the urine, the finding of other tuberculous lesions, especially in the genito-urinary tract, the positive tuberculin reaction, are all diagnostic aids which should, of course, be sought for in all doubtful cases.

Cancer and sarcoma of the kidney may, likewise, if associated with obstruction of the ureter, give rise to a cystic tumor of the abdomen combined with hæmaturia. This is certainly a comparatively rare condition, but has been repeatedly described. The pathological differentiation between carcinoma, and even sarcoma, and the suprarenal tumors, is a matter of such recent date, and even now frequently so difficult, that it is not unfair to doubt the actual nature of certain of the tumors grouped in the former category. The combination of malignant tumor in the kidney with ureteral obstruction by means of its growth, or by metastases, does, however, occur, and its differentiation from the tumors under consideration might offer certain difficulties. With the former class of tumors, the period of growth is, however, rarely so prolonged, and the cachexia generally far greater.

Calculi with partial or complete obstruction of the ureter may also give rise to recurrent hæmorrhages, and to large cystic tumors of the abdomen. The character of the urine, and the history of colic ought in these cases to render the diagnosis a matter of no great difficulty.

Tuberculosis of the ureter, new growths of the bladder obstructing the ureteral orifice, and other conditions which might simulate the symptoms of cystic hypernephromata are rare, and as a rule easily identified.

The indications for treatment are quite evident from the recital of the cases on record. The tumor is not very malignant. It is a source of danger, in the first place, as a cause of hæmorrhages and anæmia, and, in the second place, on account of the pressure symptoms which it induces in the neighboring viscera. Metastases occur, if at all, only late in the disease. Its removal is generally a simple matter and offers a radical cure. This course should, therefore, be followed in every case in which the operation is not contraindicated by the age or condition of the patient. Drainage, or repeated tapping of the cyst should never be resorted to, as these measures are not only ineffectual, but have precipitated a fatal outcome in every case in which they have been employed.

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